

## AMENDMENT TO THE CLAIMS

Please amend claim 23 and add new claims 38-42 as follows.

1. (Withdrawn) An isolated mesenchymal stromal stem cell (MSSC) that has been differentiated *in vitro* towards, or to, an intervertebral disc (IVD) cell phenotype.
2. (Withdrawn) An isolated mesenchymal stromal stem cell (MSSC) characterised in that it is:
  - a) differentiated *in vitro* towards, or to, a intervertebral disc (IVD) cell phenotype; and
  - b) genetically transformed with an exogenous gene which codes for a protein that reduces degeneration of an intervertebral disc.
3. (Withdrawn) The isolated mesenchymal stromal stem cell according to claim 1 wherein the cell produces an extracellular matrix.
4. (Withdrawn) The isolated mesenchymal stromal stem cell according to claim 3 wherein the extracellular matrix is identifiable as an IVD extracellular matrix and is distinguishable from an extracellular matrix produced by a chondrocyte.
5. (Withdrawn) The isolated mesenchymal stromal stem cell according to claim 4 wherein the IVD matrix is characterised by at least one of:
  - (a) aggrecan gene expression is greater than collagen type II gene expression;
  - (b) the proteoglycan versican is expressed; or
  - (c) the GAG: hydroxproline ratio is greater than 10:1.
6. (Withdrawn) The isolated mesenchymal stromal stem cell according to claim 1, wherein the cell is derived from blood, bone marrow, or adipose tissue.
7. (Withdrawn) The isolated mesenchymal stromal stem cell according to claim 6, wherein the cell is derived from bone marrow in the sternum, femur or iliac crest.

8. (Withdrawn) The isolated mesenchymal stromal stem cell according to claim 1, wherein the MSSC is differentiated using at least one of the steps of:
  - (a) growth in a IVD cell induction medium containing TGF $\beta$ , CDMP1 or CDMP2;
  - (b) encapsulation of the MSSC;
  - (c) application of Load to the MSSCs;
  - (d) Co-culture of the MSSC with Nucleus Pulposus cells/IVD cells;
  - (e) Culture of the MSSC in conditioned media in which IVD cells have previously been grown;
  - (f) Culture in low oxygen tensions; or
  - (g) Genetically transformed using a gene regulator of IVD cell differentiation.
9. (Withdrawn) The isolated mesenchymal stromal stem cell according to claim 8 wherein differentiation is effected by using any combination of steps (a), (b), (c), (d), (e), (f) and (g).
10. (Withdrawn) The isolated mesenchymal stromal stem cell according to claim 9 wherein the MSSC is differentiated by encapsulating the MSSC in a gel; and growing the encapsulated cell in a medium for up to 5 weeks during which time a cyclical load equivalent to that experienced *in vivo* is exerted using hydraulic or other methodology.
11. (Withdrawn) The isolated mesenchymal stromal stem cell according to claim 10 wherein the media is an induction medium according to claim 8(a).
12. (Withdrawn) The isolated mesenchymal stromal stem cell according to claim 10 wherein the media is a conditioned medium according to claim 8(e).
13. (Withdrawn) The isolated mesenchymal stromal stem cell according to claim 10 wherein the MSSC is co-cultured with cells according to claim 8(d).

14. (Withdrawn) The isolated mesenchymal stromal stem cell according to claim 11, wherein the oxygen pressure is reduced to less than 5% of the atmosphere in which the cell is cultured.
15. (Withdrawn) The isolated mesenchymal stromal stem cell according to claim 2, wherein the exogenous gene is selected from the group consisting of genes encoding proteins involved in the regulation of inflammation, genes encoding cytokines, genes encoding inhibitors of cytokines, and genes encoding inhibitors of degradative enzymes.
16. (Withdrawn) The isolated mesenchymal stromal stem cell according to claim 2, wherein the exogenous gene encodes Interleukin 1 Receptor Antagonist (IL-1RA).
17. (Withdrawn) A composition for the treatment of spinal conditions characterized by degeneration of the intervertebral disc, comprising the mesenchymal stromal stem cell of claim 1.
18. (Withdrawn) The composition according to claim 17 wherein the spinal condition is Low Back Pain, degeneration of the intervertebral disc, age-related changes of the intervertebral disc or spondylolysis.
19. (Withdrawn) The composition according to claim 17 wherein the composition is configured for direct injection into an IVD exhibiting DVID.
20. (Withdrawn) The composition according to claim 17 wherein the composition is configured for seeding onto or into biomaterial scaffolds or gels.
21. (Withdrawn) A method of treating spinal conditions characterized by degeneration of the intervertebral disc comprising:
  - providing a composition comprising an isolated MSSC that has been differentiated *in vitro* towards, or to, an IVD cell phenotype; and
  - administering said composition to a diseased intervertebral disc of a subject in need of such treatment.

22. (Withdrawn) A method of treating spinal conditions characterized by degeneration of the intervertebral disc comprising:  
providing a composition comprising an isolated MSSC, wherein said MSSC has been:  
(a) differentiated *in vitro* towards, or to, a IVD cell phenotype,  
and  
(b) genetically transformed with an exogenous gene which codes for a protein that reduces degeneration of an intervertebral disc;  
and  
administering said composition to a diseased intervertebral disc of a subject in need of such treatment.
23. (Currently Amended) A method for causing human mesenchymal stromal stem cells to differentiate towards IVD cells comprising exposing cultured mesenchymal stromal stem cells, encapsulated in a gel, to increasing pressures of up to 30 psi (2.1MPa) and reduced oxygen tension.
24. (Withdrawn) A method for causing mesenchymal stromal stem cells to differentiate towards IVD cells comprising co-culturing NP cells and mesenchymal stromal stem cells (MSSCs) together.
25. (Withdrawn) A method for causing mesenchymal stromal stem cells to differentiate towards IVD cells comprising culturing mesenchymal stromal stem cells in media that has previously been exposed to NP cells.
26. (Withdrawn) A method for causing mesenchymal stromal stem cells to differentiate towards IVD cells comprising culturing mesenchymal stromal stem cells in an atmosphere in which oxygen pressure is reduced to less than 5%.
27. (Withdrawn) A method for causing mesenchymal stromal stem cells (MSSCs) to differentiate towards IVD cells comprising encapsulating MSSCs in a gel and growing the encapsulated cells in a medium for up to 5 weeks during which time

a cyclical load equivalent to that experienced *in vivo* is exerted using hydraulic or other methodology

28. (Withdrawn) The method according to claim 27 wherein the media is an induction medium containing TGF $\beta$ , CDMP1 or CDMP2.
29. (Withdrawn) The method according to claim 27 wherein the media is a conditioned medium in which IVD cells have previously been grown.
30. (Withdrawn) The method according to claim 27 wherein the MSSCs are co-cultured with Nucleus Pulposus cells/IVD cells.
31. (Withdrawn) The method according to claim 27 wherein the oxygen pressure is reduced to less than 5% of the atmosphere in which the cells are cultured.
32. (Withdrawn) The method according to claim 28 wherein the oxygen pressure is reduced to less than 5% of the atmosphere in which the cells are cultured.
33. (Withdrawn) The method according to claim 29 wherein the oxygen pressure is reduced to less than 5% of the atmosphere in which the cells are cultured.
34. (Withdrawn) The method according to claim 30 wherein the oxygen pressure is reduced to less than 5% of the atmosphere in which the cells are cultured.
35. (Withdrawn) The isolated mesenchymal stromal stem cell according to claim 2 wherein the cell produces an extracellular matrix.
36. (Withdrawn) The isolated mesenchymal stromal stem cell according to claim 12, wherein the oxygen pressure is reduced to less than 5% of the atmosphere in which the cell is cultured.
37. (Withdrawn) The isolated mesenchymal stromal stem cell according to claim 13, wherein the oxygen pressure is reduced to less than 5% of the atmosphere in which the cell is cultured.

- 38. (New) The method according to claim 23 wherein, the gel is an alginate gel.
- 39. (New) The method according to claim 23 wherein, the reduced oxygen tension is 0.1% - 20% O<sub>2</sub>.
- 40. (New) The method according to claim 23 wherein, the reduced oxygen tension is less than 10% O<sub>2</sub>.
- 41. (New) The method according to claim 23 wherein, the reduced oxygen tension is less than 5% O<sub>2</sub>.
- 42. (New) The method according to claim 23 wherein, the reduced oxygen tension is about 1% O<sub>2</sub>.